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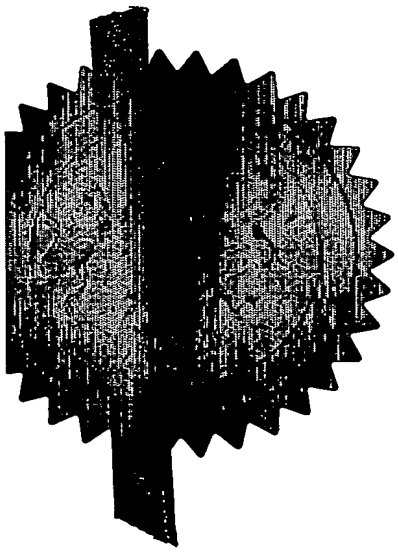

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CRANFIELD UNIVERSITY
CRANFIELD
BEDFORDSHIRE, MK43 0AL, UK

Patents ADP number *(if you know it)* 64588648007

If the applicant is a corporate body, give the country/state of its incorporation

4. Title of the invention SUBSTANCE-SELECTIVE POLYMER MEMBRANES

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

LINDA TIDWELL
CRANFIELD UNIVERSITY
SILSOE
BEDFORDSHIRE, MK45 4DT, UK

Newburn Ellis,
York House,
23 Kingsway,
London WC2B 6HP

Patents ADP number *(if you know it)* 8321077001

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*
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Description	10 (PAGES 2-11)
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FIELD OF THE INVENTION

The present invention relates generally to synthesis and application of polymeric membranes for solid-phase extraction, separation, purification and sensing of organic molecules.

BACKGROUND OF THE INVENTION

Over the last three decades, new molecular imprinting approaches for introducing affinity binding sites into synthetic polymers have been developed [1, 2]. In this technique highly cross-linked polymer is formed around a template molecule. The template is then removed by washing and a cavity with functional groups complementary to these of template molecule remains behind in a polymer. It has been shown that molecularly imprinted polymers (MIPs) can be developed for variety of compounds [3, 4] and their synthesis is straightforward and inexpensive procedure. These polymers demonstrate very good thermal and mechanical stability and can be used in aggressive media [5]. Therefore, the molecular imprinting approach allows one to combine the ability of natural receptors to selectively bind the analyte with the stability and robustness of synthetic polymers.

MIPs have been widely used as a stationary phase for chromatographic separation [6, 7], as substitutes for antibodies in immunoassays [8, 9], and as selective elements for electrochemical sensors [10, 11] and solid-phase extraction (SPE) [12–14].

Chromatographic and SPE applications traditionally utilise MIP particles prepared by grinding and sieving of synthesised polymer blocks or particles prepared by suspension polymerisation. The first approach is time consuming, might lead to destruction of some binding sites in the polymer and produces a relatively low yield of fraction with a narrow size distribution as required for the practical application. In the second approach, the choice of monomers is limited to those which are not soluble in the dispersion phase. Additionally the synthesised beads are also not uniform in their shape and size. Therefore, again a tedious sieving procedure is required to obtain uniformly sized particles for packing. As a result, the

packing of a column with MIP is time-consuming, expensive and ineffective. Other less conventional approaches to improve the quality of HPLC materials and facilitate the preparation procedure have been tried. Thus Kumakura et al. [15] disclose a porous polymer composite column produced by radiation casting polymerisation. Matsui et al. [16] describe the preparation of porous MIP rods *in situ* inside HPLC columns. This approach, however suffered from quality control problems (too many synthesised columns have defects) and often too high a backpressure. Potentially chromatography can be performed on membranes. For example, U.S. Patents 4,889,632, 4,923,610 and 4,952,349 disclose chromatography on thin layer macroporous membranes punched from a macroporous sheet of polymer. The difficulty in designing MIP membranes for chromatography and filtration is twofold: the high level of cross-linking, traditionally used in molecular imprinting results in the formation of too fragile and brittle a membranes and in a relatively low porosity, which prevents their use in chromatography due to high backpressure. The problem of membrane fragility has been resolved by adding plasticiser to the polymer composition - oligourethane acrylate [17]. The casted membranes were flexible, but their porosity was too low for chromatographic separation.

The present invention is focused on development of imprinted membranes, which are mechanically stable, flexible and porous and suitable for application in filtration and chromatography.

DESCRIPTION OF THE INVENTION

In general, the present invention describes a flexible porous membrane made of molecularly imprinted polymer. The MIP membrane is useful as a chromatographic media and it will also find application in various separation, catalytic, diagnostic, and absorption processes due to its affinity, selectivity and ability to pass liquids therethrough. The polymer contains not only small pores, i.e. those below about 100 nm in diameter, but also large pores, i.e. those at least

500 nm in diameter. The flexible porous MIP membrane is produced by co-polymerisation of functional monomers and a cross-linker in the presence of a template, plasticiser (non-extractable component), pore-forming component (extractable component) and initiator. The polymerisation is performed in a thin layer, which in some aspects will be confined between the transparent or non-transparent articles, which will define the geometry, to some degree morphology and thickness of the formed film. The extractable pore-forming component, template, non-reacted monomers, cross-linker, plasticiser and initiator is then removed with a suitable solvent.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 describes the dependence of the atrazine-imprinted (MIP) and reference (Blank or control) membrane sorption capability on the concentration of atrazine in the feed solution: 10 ml of the solution were passed across the membranes at a rate of 0.5 ml/min at pressure 2430 PSI.

DETAILED DESCRIPTION OF THE INVENTION

The first embodiment of the present invention describes the composition used for preparation of flexible and porous MIP membrane, which contains: functional monomers, tempate, crosslinker, plasticiser (non-extractable component), pore-forming component (extractable component) and initiator. The role of functional monomers lies in providing functionalities capable of interacting with template through, preferably electrostatic (ionic and hydrogen bond), van-der-Waals, dipole-dipole, charge transfer, reversible covalent or hydrophobic interactions. Template interacts with functional monomers and forms a complex, which will be integrated into the polymer network formed during polymerisation. Template directs positioning of functional monomers and creates into the resulting polymer specific binding sites - imprints. The role of cross-linker lies in the formation of three-dimensional network

capable of preserving some structural features of the monomers and their orientation as it exists in the complex formed with template. The cross-linked polymer network will maintain and preserve the imprints (cavities with a shape and orientation of functional groups complementary to those of the template molecules). The role of the plasticiser lies in providing a certain level of flexibility to an otherwise rigid polymer network. In some aspects the plasticiser will be co-polymerised with the monomers and cross-linker forming a covalently bound network, in other aspects the plasticiser will form only physical bonds (interpenetrated polymer network) with monomers and cross-linker. The role of the pore-forming component lies in the formation large open and close pores in the polymer matrix, suitable for effective transport of solution, which is required for chromatographic application of these membranes. The initiator generates free radicals (in radical polymerisation) or ions (in ionic polymerisation).

Suitable monomers and cross-linker are selected from the group consisting of vinyl, allyl, styrene, acrylic or methacrylic derivatives, with non-exclusive examples of divinylbenzene, divinylnaphthalene, vinylpyridine, hydroxyalkylene methacrylates, ethylene glycol dimethacrylate, vinyl esters of carboxylic acids, divinyl ether, pentaerythritol di-, tri-, or tetramethacrylate or acrylate, trimethylopropane trimethacrylate or acrylate, alkylene bis acrylamides or methacrylamides, methacrylic and acrylic acid, acrylamide, hydroxyethyl methacrylate, and their mixtures. The monomers and cross-linker are generally present in the polymerisation mixture in an amount of from about 10 to 80 vol. %, and more preferably in an amount of from about 40 to 80 vol. %.

The template is selected from a group including biological receptors, nucleic acids, immunosuppressants, hormones, heparin, antibiotics, vitamins, drugs or synthetic molecules possessing biological activity, cell components and components of viruses such as

carbohydrates, lipids, saccharides, nucleoproteins, mucoproteins, lipoproteins, peptides and proteins, glycoproteins, glucosaminoglycanes and steroids.

The pore-forming component is selected from a variety of different types of materials, including aliphatic hydrocarbons, aromatic hydrocarbons, esters, alcohols, ketones, ethers, butyl alcohols, isobutyl alcohol, dimethyl sulfide, formamide, cyclohexanol, saccharose acetate isobutyrate, H_2O, glycerol, sodium acetate, solutions of soluble polymers, and mixtures thereof. Suitable soluble polymers used herein include non-cross-linked polymers or copolymers of such monomers as styrene or ring substituted styrene, acrylates, methacrylates, dienes, vinylchloride, and vinylacetate, polyvinyl chloride, polyethylene glycol, polyvinylpyrrolidone, polyvinyl alcohol, cyclohexanol, mineral oil, etc. The pore-forming component is present in the monomer mixture in an amount of from 5 to 60 vol %.

A plasticiser is polymerisable or non-polymerisable compound of oligomeric or polymeric nature, selected from variety of different types of materials including, as non-exclusive examples, oligourethane acrylate, butadiene (or isoprene) rubber, polyurethane, caoutchoucs, etc. The amount of the plasticiser can vary from 5 to 50% (by weight) in the monomer mixture, preferably 5–20%.

Conventional free-radical generating polymerisation initiators may be employed to initiate polymerisation. Examples of suitable initiators include peroxides such as OO-t-amyl-O-(2ethylhexyl)monoperoxycarbonate, dipropylperoxydicarbonate, and benzoyl peroxide, as well as azo compounds such as azobisisobutyronitrile, 2,2'-azobis(2-amidinopropane)dihydrochloride, 2,2'-azobis(isobutyramide)dihydrate and 1,1'-azobis (cyclohexane carbonitrile). The initiator is generally present in the polymerisation mixture in an amount of from about 0.01 to 5% by weight of the monomers.

In some aspects the composition will contain also solvent (ethylacetate, methyl ethyl ketone, acetone, dimethylformamide, toluene, dioxane, chloroform), added for improvement of

components compatibility, improvement of the homogeneity of monomer mixture, facilitating complexation between monomers and template or for regulation polymer porosity (making it more or less porous) through the modification of the phase separation process during polymerisation.

In some aspects the composition includes matrix made of insoluble polymer, glass or ceramic matrix, soaked with an inhibitor, which inhibits free radical polymerisation. This will help to create voids around of solid matrix, which will be free of polymer and suited for transport of liquids and analytes. Suitable inhibitors include cupric chloride and sodium nitrite. The inhibitor is generally present in an amount of from about 0.001 to 1 wt %, based on the total weight of solid matrix.

The second embodiment of the present invention describes the preparation of flexible and porous MIP membranes. The process generally comprises four steps:

- mixing components and their degassing;
- forming a thin layer of mixture by: a) confining it between articles which restrict its expansion and defines the geometry and shape of resulting membrane or b) by pouring membranes onto the surface in such a way that its becomes flat under gravity;
- polymerising the mixture to form a solid porous membrane;
- washing the membrane with a solvent so as to remove pore-forming component, template, non-reacted monomers, cross-linker, plasticiser and initiator.

The degassing of the mixture (needed for removal of oxygen and other dissolved gases) is achieved by conventional means such as purging an inert gas such as nitrogen through the solution for a sufficient period of time. If the following polymerisation is performed in thin layer between the transparent or non-transparent articles, then these articles will define the geometry and to some degree the morphology and thickness of the formed film.

The polymerisation is carried out in a conventional manner, generally at a temperature of about 40 -100 °C for a period of from about 1 to 24 hours, depending on the initiator and monomers used. In a preferable method the polymerisation is performed using UV irradiation at temperature in the range of -30 °C to + 60 °C.

After polymerisation is complete, the membrane is washed to remove the pore-forming component, template, non-reacted monomers, cross-linker, plasticiser and initiator with a suitable solvent. Non-exclusive examples of suitable washing solvents include methanol, ethanol, benzene, toluene, acetone, tetrahydrofuran, dioxan, acetonitrile, water or their mixtures. In some aspects the washing solvent will include additives suitable for weakening template-functional monomer complexes, e.g. acid, base, salt, surfactant or chaotropic agents. The polymeric membrane synthesised as described above contains small pores (< 100 nm), and large pores (> 500 nm). The large pores are preferably from about 800 to 2,500 nm in diameter. The large pores represent at least 10% of the total pore volume of the membrane in order to achieve a reasonable flux in chromatographic separation. The small pores generally have sizes in the range 0.1 to 200 nm. The synthesised membrane has a balance of appropriate macroporosity and physical strength to allow a liquid to pass through it under a pressure of less than 8000 PSI at a linear flow rate of at least 0.5 ml/min.

The third embodiment of the present invention describes an application of flexible and porous MIP membranes synthesised as described above. Some aspects of the present invention include the use of the synthesised membranes as a separation matrix in membrane chromatography. Yet another aspect includes the use of these membranes in catalytic, diagnostic or absorption processes, e.g. in solid phase extraction in accordance with conventional techniques known in the art.

Examples

The Examples are intended to illustrate, but not limit, the scope of the invention.

Example 1.

Synthesis of flexible and porous molecularly imprinted polymer membranes.

In an exemplary embodiment, the porous thin and flexible MIP membrane is synthesised from the mixture of monomers including atrazine as a template (40 mg), methacrylic acid as a functional monomer (80.4 mg), tri (ethylene glycol) dimethacrylate as a cross-linking agent (616.6 mg), oligourethane acrylate as a plasticiser (102.9 mg), polyethylene glycol as a por-forming component (120 mg), dimethylformamide (50 vol%) as solvent and 1,1'-azobis (cyclohexane carbonitrile) as an initiator of polymerisation (40 mg). The mixture was poured between two glass slides with a fixed distance between them of 60 μm and polymerisation was initiated by either UV-irradiation (λ=365 nm) or was carried out at 80°C for 1 hour. Reference polymeric membranes were synthesised with the same mixture of monomers, but in the absence of the template. To remove the template molecules and non-reacted monomers, cross-linker etc. and polyethylene glycol, the membrane was extracted with hot methanol in Soxhlet apparatus for 8 hours followed by washing in a hot water for the other 8 hours. The Blank membrane was prepared in the same way with exception that atrazine-template was absent in the polymer composition.

Example 2.

Use of molecularly imprinted polymer membranes in solid-phase extraction of triazine herbicides.

A membrane synthesised as describe in Example 1 and with a diameter of 5 mm was placed between two chambers of a separation cell and a diluted solution of atrazine was passed across the membrane at a rate 0.5 ml/min. The membrane recognition properties were

evaluated by measuring their capacity to adsorbed atrazine from aqueous solutions (10^{-8}–10^{-5} M). The herbicide concentration in both feed and permeate solutions were determined using Gas Chromatography-Mass Spectrometry(GC/MS). The membranes demonstrated high adsorption ability towards atrazine together with negligible binding of atrazine to Blank membranes (Fig. 1)

Example 3

Synthesis of membranes imprinted with ephedrine for separation of structurally similar compounds in HPLC mode.

In an exemplary embodiment, the porous thin and flexible membrane is synthesized from the mixture of monomers including ephedrine (+) as a template (40 mg), hydroxyethyl methacrylate as a functional monomer (299 mg), tri (ethylene glycol) dimethacrylate as a cross-linking agent (1106 mg), oligourethane acrylate as a plasticiser (195 mg), mixture of toluene (50 vol%) and mineral oil (160 mg) as a porogen, and 1,1'-azobis (cyclohexane carbonitrile) as an initiator of polymerisation (80 mg). The mixture was poured between two glass slides with the fixed distance between them of 60 μm and polymerisation was initiated by either UV-irradiation (λ=365 nm) or was carried out at 80°C for 1 hour. Reference polymeric membranes were synthesised with the same mixture of monomers, but in the absence of the ephedrine (+). To remove the template molecules, non-polymerised compounds, and mineral oil, the membrane was extracted with chloroform for 24 hours. The membrane synthesised (diameter 5 mm) was placed between two chambers of the separation cell and was used instead of a chromatography column filled with particles. The cell was used for the separation of ephedrine (+) and ephedrine (–) and detection was performed using UV-absorbance at 260 nm. At flow rate 1 ml/min at HPLC system pressure of 3000 PSI was observed.

References

Patent	Country	Issued	Title
5,334,310	USA	August 2, 1994	Column with macroporous polymer media
4,889,632	USA	December 26, 1989	Macroporous polymeric membranes for the separation of polymers and a method for their application
4,923,610	USA	May 8, 1990	Macroporous polymeric membranes for the separation of polymers and a method for their application
4,952,349	USA	August 28, 1990	Macroporous polymeric membranes for the separation of polymers and a method for their application

Other references:

1. G. Wulff, Angew. Chem. 107 (1995) 1958.
1. A.G. Mayes, K. Mosbach, Trends Anal. Chem. 16 (1997) 321.
2. O. Ramstrom, I.A. Nicholls, K. Mosbach, Tertahedron Assym. 5 (1994) 649.
3. M. Siemann, L.I. Andersson, K. Mosbach, J. Agric. Food. Chem. 44 (1996) 141.
4. D. Kriz, K. Mosbach, Anal. Chim. Acta 300 (1995) 71.
5. G. Wulff, S. Schauhoff, J. Org. Chem. 56 (1991) 395.
6. P.K. Owens, et al. Trends. Anal. Chem. 18 (1999) 146.
7. P.K. Owens, et al. Trends. Anal. Chem. 18 (1999) 146.
8. G. Vlatalis, et al. 361 (1993) 645.
9. S.A. Piletsky, et al. Biosens. & Bioelectron. 10 (1995) 959.
10. T.A. Sergeyeva, et al., Analyst 124 (1999), 331.
11. C. Baggiani et al. J. Cromatogr. A, 938, (2001), 35.
12. K. Moller, U. Nilsson, C. Crescenzi, J. Cromatogr. A, 938, (2001), 21.
13. K. Jinno et al. J. Cromatogr. A, 754, (1996), 137.
14. D.K. Roper, E.N. Lightfoot, J. Chromatogr. A, 702 (1995), 171.
15. Kumakura et al. J. Mat. Sci. 24 (1989), 1809.
16. J. Matsui et al. Anal. Chem. 65 (1993), 2223.
17. T. A. Sergeeva et al. Anal. Chim. Acta 392 (1999), 104.

Claims

What is claimed is:

1. A method for synthesis of a substrate-selective membrane where template, functional monomers, cross-linker, plasticiser and pore-forming component are mixed together and polymerised. Extraction of the template and porogen leads to the formation of a thin, flexible and porous polymeric membrane.
2. A substrate-selective membrane prepared as in Claim 1, containing small (< 100 nm in diameter) and large (> 500 nm in diameter) open and close pores with some of the small pores having a shape and arrangement of functional groups complementary to the template molecule.
3. The membrane of Claim 1, wherein the polymer has a porosity of from about 25 to 90%.
4. The membrane of Claim 1 wherein the monomers and cross-linker are selected from the group consisting of vinyl, allyl, styrene, acrylic or methacrylic derivatives, and mixtures thereof.
5. The membrane of Claim 1, wherein the plasticiser is selected from the group consisting of polymerisable or non-polymerisable compound of oligomeric or polymeric nature, selected from variety of different types of materials such as oligourethane acrylate, butadiene (or isoprene) rubber, polyurethane, caoutchoucs, etc.
6. The membrane of Claim 1, wherein the pore-forming component is selected from the group of aliphatic hydrocarbons, aromatic hydrocarbons, esters, alcohols, ketones, ethers, solutions of soluble polymers, and mixtures thereof. Suitable soluble polymers used herein include non cross-linked polymers or copolymers of such monomers as styrene or ring substituted styrene, acrylates, methacrylates, dienes, vinylchloride, and vinylacetate, polyvinyl chloride, polyethylene glycol, glycerol, cyclohexanol, mineral oil, etc.

7. The membrane of Claim 1, wherein the pore-forming component is selected from the group consisting of insoluble macroporous polymer particles which are cross-linked copolymers of the monomers of Claim 4 with a diameter 1–1000 micrometers.
8. The membrane of Claim 1, wherein the pore-forming component is selected from the group consisting of inorganic porogens including $Mg(Cl_4)_2$, $ZnCl_2$, $CaCl_2$, SiO_2, $NaNO_3$, $NaOCOCH_3$, NaCl.
9. The application of membrane synthesised according to Claim 1 as a separation matrix in membrane chromatography, catalytic, diagnostic, or absorption processes, e.g. in solid phase extraction.

Substance-selective polymer membranes

ABSTRACT: Broadly the present invention describes synthesis of highly porous substance-selective polymeric membranes and their application in analytical chemistry, pharmacology, medicine, the food industry, water purification and environmental clean up. The method includes co-polymerisation of functional monomers and cross-linker in the presence of template, plasticiser (non-extractable component), and pore-forming component (extractable component). Extraction of the template and porogen molecules leads to the formation of small (< 100 nm in diameter) and large (> 500 nm in diameter) open and close pores with some of the small pores having a shape and arrangement of functional groups which is complementary to the template molecule. The synthesised molecularly imprinted polymeric (MIP) membranes possess enhanced affinity towards the template and its analogues and also have high flexibility and porosity, which is important for their practical applications. As a further aspect of the present invention, substrate-selective polymeric membranes, synthesised as described above, can be used in analytical chemistry (as sensor elements and for solid-phase extraction materials) for applications in pharmacology, medicine, the food industry, water purification and environmental clean up.

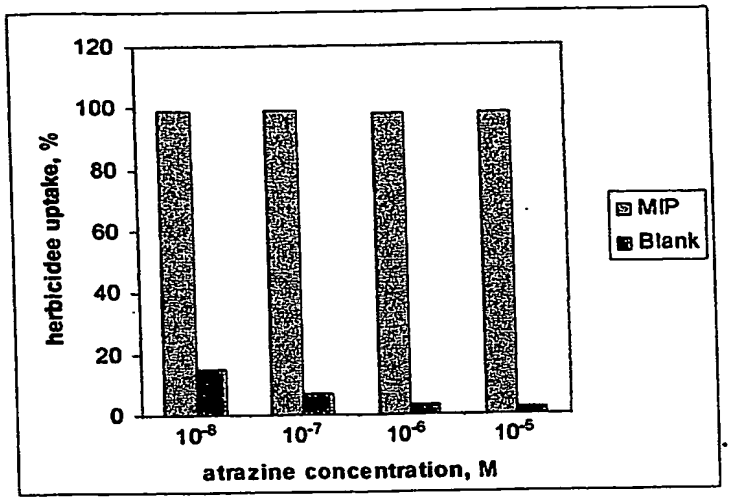

Fig. 1. Dependence of the atrazine-imprinted (MIP) and reference (Blank) membrane sorption capability on the concentration of atrazine in the feed solution: 10 ml of the solution were passed across the membranes at a rate 0.5 ml/min at pressure 2430 PSI.

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